## REMARKS

Applicants appreciate the through examination of the present application as evidenced by the Office Action dated June 30, 2005 (hereinafter, "the Office Action"). Claims 12, 15, 19-21, 23-26 and 31-35 are pending in the present application upon entry of the present Amendment. The concerns raised by the Examiner in the Office Action are addressed below.

### I. Interview Summary

Applicants wish to express their appreciation to the Examiner for the courtesy extended to Dr. Sigounas and Applicants' legal representative, Shawna Cannon Lemon, during the in-office interview on August 11, 2005. Applicants further wish to express their appreciation for the considerable time and effort expended by the Examiner during the interview.

During the interview, Dr. Sigounas and the Examiner discussed various aspects of the invention and the cited art.[1] Dr. Sigounas reviewed the background and history of the problem to be solved, *i.e.*, treating solid vascularized tumors. Dr. Sigounas also discussed the treatment protocols associated with treatment of anemic cancer patients who are administered erythropoietin (EPO) to treat anemia and contrasted this protocol with the current regimen directed to using (EPO) to treat solid vascularized tumors. The Examiner and Dr. Sigounas further discussed several references, presently or previously cited, and their relationship to the present invention.

At the conclusion of the interview, the Examiner requested that evidence directed to (a) *in vivo* data supporting the use of EPO to treat solid vascularized tumors, (b) the relationship of various cancers and anemia, and (c) the timing of administration of EPO and chemotherapeutic agents be provided in the form of a Declaration. The Examiner indicated that she would review the written documents prior to making a final determination. Applicants submit herewith a Declaration Under 37 C.F.R § 1.132 of George Sigounas, Ph.D. (hereinafter, the "Sigounas Declaration") pursuant to the Examiner's request.

### II. Claim Rejections Under 35 U.S.C. §§ 103 and 102

Claims 12-15, 19-21, 23-26 and 31-33 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Bukowski et al. *Blood.* **84** (No. 1, Suppl. 1): 129a (1994)

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[1] A portion of the interview was also attended by Examiner Christopher H. Yaen. Examiner Yaen is the Examiner of record for related application U.S. Patent Application Serial No. 09/525,808 (Attorney Docket No. 5218-39C).

(hereinafter, "Bukowski et al.") for reasons previously set forth in the paper mailed January 28, 2005, Section 9, pages 7-9. *See* Office Action, page 2.

Claims 12-15, 19-21, 23-27 and 31-33 remain rejected under 35 U.S.C. §102(b) as being unpatentable over Bukowski et al. for reasons previously set forth in the paper mailed December 28, 2004, Section 6, pages 3-7 and further for the reasons set forth in the current Office Action. *See* Office Action, page 3. In particular, the Office Action states that "it is clear that the treatment protocol [of Bukowski et al.] is a pan cancer treatment protocol across a wide variety of cancers, including any and all solid vascularized tumors and thus the instant reference anticipates this treatment for any and all cancers including any and all solid vascularized tumors." Office Action, page 3.

Applicants respectfully submit that the pending claims are neither obvious nor anticipated in view of the cited references for at least the reasons set forth herein.

As noted in the Sigounas Declaration, one aspect of Applicants' research relates to the study of erythropoietin (EPO) as a potentiator of chemotherapy. The present specification provides *in vitro* data in support of the ability of EPO to decrease endothelial cell proliferation and viability, and the Sigounas Declaration sets forth *in vivo* data in support of the same through experiments that show the ability of EPO to reduce tumor size and volume.

None of the cited references teach or suggest the recitations of currently amended independent Claims 12 and 21. As noted in the Sigounas Declaration, cancer patients typically receive EPO only after being diagnosed with anemia. Thus, references directed to administration of EPO to anemic cancer patients do not teach or suggest **providing erythropoietin prior to administration of a chemotherapeutic agent**, wherein said erythropoietin is administered in an amount effective to enhance suppression of endothelial growth associated with administration of said chemotherapeutic agent as recited Claim 1, or further wherein said erythropoietin is administered **in an amount of from about 750 Units per kilogram to about 2,000 Units per kilogram** as recited in Claim 21, which Applicants indicate as an amount of EPO capable of enhancing suppression of endothelial growth caused by a chemotherapeutic agent. *See* Present Application, page 12, lines 32-37.

Results of the *in vivo* experiments carried out by and under the direction of Dr. Sigounas show that in a treatment group wherein animals were injected sequentially first with EPO and then with a designated chemotherapeutic drug, the tumor mass in animals treated with EPO followed by cisplatin was reduced by 4.0-fold compared to saline-injected animals

and was 1.6 times less than the tumor mass in animals treated with cisplatin alone. *See* Tab 8 of the Sigounas Declaration. Sequential administration of EPO and mitomycin C (MITO) showed a reduction in tumor mass compared to the reduction observed with MITO alone, however, this difference was not statistically significant (data not shown).

In view of the claim amendments and the experimental data presented in the specification and further supported by the Sigounas Declaration, in contrast to the assertions of the Office Action on page 5, Applicants respectfully submit that the method of the cited references do not comprise the same method steps recited in the pending claims and that the presently recited methods are not anticipated because the method discussed in the cited references would not inherently lead to enhanced suppression of endothelial growth associated with administration of cisplatin. As noted above, and further explained in detail in the Sigounas Declaration, anemic cancer patients typically do not receive EPO **prior** to chemotherapy. Accordingly, prior to the Applicants' discovery, there was no motivation to provide EPO to cancer patients other than to treat anemia and only **after** initiation of chemotherapy.

Applicants further respectfully submit that one of ordinary skill in the art would not have a reasonable expectation of success of treating patients with cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx using the protocol described in Bukowski et al. As noted in Applicants' previous response dated March 28, 2005, the patients described in Bukowski et al. are anemic cancer patients, and further, Bukowski et al. alleges that a non-specific cancer patient population experienced improved energy level, activity level and overall well-being. These clinical outcomes are indications that their anemic condition may have improved, which is the focus of the Bukowski et al. study. Even more significantly, however, as noted in the Sigounas Declaration, solid vascularized tumors are **not** typically associated with anemia at the time of cancer diagnosis and/or chemotherapy. Accordingly, one of ordinary skill in the art would not have a reasonable expectation of success of treating solid vascularized tumors selected from cerebellar hemangioblastoma, ductal carcinoma of the breast or squamous cell cancer of the larynx as recited in new Claims 34 and 35.

Other previously cited references such as *Proc. Am. Soc. Clin. Oncol.* 1994, 13, 30 Meet, 234. to Bokkel et al. and JP 02 096535 to Chugai Pharmaceutical Co. Ltd. do not supply the missing recitations or provide the motivation to administer EPO in the manner

recited in the pending claims.

At least in view of the foregoing, Applicants respectfully submit that Claims 2, 15, 19-21, 23-26 and 31-35 are patentable, and Applicants respectfully request withdrawal of the claim rejections.

## Conclusion

Applicants respectfully submit that, for the reasons discussed above, the references cited in the present rejections do not disclose or suggest the present invention as claimed. Accordingly, Applicants respectfully request allowance of all the pending claims and passing this application to issue.

It is not believed that any fee(s), including fees for additional claims, are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that additional fees are necessary to allow consideration of this paper, such an extension is also hereby petitioned for under 37 C.F.R. §1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,

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**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on October 31, 2005.

Susan E. Freedman

Susan E. Freedman
Date of Signature: October 31, 2005